Syphilis and Parasyphilis of the Nervous System.

By F. W. Mott, M.D., F.R.S.

The causal connexion of tabes dorsalis and general paralysis with syphilis is now so firmly established in the minds of most neurologists that it would be absurd, in dealing with such an important question as syphilis of the nervous system, not to include these parasyphilitic affections. Diseases of the nervous system due to syphilis may then be classified thus :—

(I) (*a*) *Syphilitic diseases of the brain*, comprising the following forms : Basic meningitis, meningitis of the convexity, cerebrospinal meningitis, arteritis, and, lastly, gummatous tumours. My experience, indicated by a large number of recorded cases in which autopsies were performed, shows that all these conditions may be more or less combined in the severe and early forms of the disease. (*b*) *Syphilitic diseases of the spinal cord.*

These diseases are all due to the direct effects of the syphilitic virus upon the mesoblastic nutrient, enclosing and supporting tissues of the central nervous system, causing secondary degenerative changes in the essential nervous elements.

(II) *Parasyphilitic affections :* (*a*) Tabes dorsalis ; (*b*) Tabes optica ; (*c*) Paralytic dementia.

In syphilitic disease of the nervous system we divide our cases into spinal and cerebral for clinical convenience, but my experience as a

pathologist tends to show that the whole cerebrospinal axis is usually, if not always, affected, although in some cases the spinal symptoms are the most obtrusive, and in others the cerebral; and that leads me to the consideration of the relation of syphilitic eruption of the skin to recognized and unrecognized syphilis of the meninges. Many cases of syphilis of the meninges could be cited where the symptoms have appeared within three months of the primary infection—e.g., one of the cases reported by Goldflam. A strong man, aged 40, one month after the appearance of an indurated chancre, was seized with violent pains in the neck, the shoulders, and upper limbs, with stiffness and immobility of the limbs. There was also a marked hyperæsthesia in the area supplied by the brachial plexus. The case was completely cured after twenty-four inunctions.

The following cases in my own practice are instructive: (1) A young man was sent to me complaining of headache, internal strabismus, and double vision; he had also commencing optic neuritis. I ascertained that ten weeks previously he had contracted a so-called soft sore, which had been treated only locally with iodoform. I put him on mercurial inunction, and the symptoms rapidly left him. (2) A man was admitted to Charing Cross Hospital, under my care, who, thirty years previously, had suffered with chancre, sore throat, and rash; and *was reinfected sixteen months ago.* He again had a chancre, rash, and sore throat. Within twelve months of infection he suffered with girdle pain on the left side, absence of abdominal reflex, and some root anæsthesia on this side, increase of the deep reflexes and slight Babinski on this side, together with inability to empty the bladder. He had a papular rash on admission, and general polyadenitis. There was a lymphocytosis of the cerebrospinal fluid not marked. He improved rapidly on mercurial inunction. The rash rapidly cleared up, and the local symptoms also. The case, therefore, was a localized syphilitic meningitis due to reinfection. This case is interesting, for it is rare to find a case of reinfection.

Sir William Gowers, in his Lettsomian Lectures, 1890, scathingly criticized the evidence brought forward by Long and others to show that a slight meningitis may be associated with the early phenomena of syphilis more frequently than was generally supposed. But the modern conception of the cause of the roseolar rash by the spirochæte of syphilis escaping from the blood in the cutaneous vessels makes it possible that a similar infection of the cerebrospinal meninges may occur.

The researches of Ravaut and others show the frequent existence of a lymphocytosis during the secondary period, sometimes very abundant, which proves there may be a meningeal reaction concomitant to the cutaneous eruption. A series of observations of lymphocytosis of the cerebrospinal fluid of early cases of syphilis, in which there occurred slight signs of meningeal irritation and a parallelism between the abundance of lymphocytes and the intensity of the signs of meningeal irritation, both disappearing and diminishing under treatment, would substantiate Long's hypothesis. Boidin and Pierre Weil point out that the study of the cerebrospinal fluid shows that the central nervous system is very frequently affected in the secondary period, but this affection may only be habitually shown by the cellular reaction of the meninges, and is sometimes associated with ocular troubles or paralysis of cranial nerves or other objective signs; it is exceptional, however, for signs of acute meningitis to recur. They describe the case of a young man, aged 18, admitted to the hospital with all the signs of an acute meningitis—headache, vomiting, constipation, rigidity of neck, Kernig's sign, inequality of pupils, and slight elevation of temperature. The first impression was that it was a case of tubercular meningitis, but upon examination of the patient the existence of an indurated chancre of the penis was discovered. No other specific sign was found; no mucous plaques, no roseola, no suboccipital adenopathy. Lumbar puncture revealed a pure lymphocytosis of average intensity; four days later the roseolar rash appeared. This patient rapidly recovered under treatment, and the following is a chronology of the symptoms: (1) Chancre, middle of June; (2) headache, July, 15; (3) signs of meningitis, August 5; (4) roseola, August 12; (5) cure of the meningitis, August 15.

The living organism in the blood presumably may, in rare instances, affect the blood-vessels of the meninges before the blood-vessels of the skin; occasionally the meninges are affected simultaneously with the skin, causing a sufficient degree of irritation to lead to manifest symptoms. But just the same as the roseolar rash may be so slight as to escape observation, so the eruption in the meninges may be so slight as to cause no symptoms; but if the meninges are infected, it is quite possible that the virus may remain latent until some other cause acts as a co-efficient in the production of a definite lesion with symptoms. The following case occurred in my practice and illustrates this point: A soldier, aged 28, contracted syphilis; eighteen months later he was thrown from his horse and he felt considerable pain in the back, but

was able to walk after the accident, and he observed no symptoms for a week; then he felt a tightness in the lower part of the abdomen, weakness in the legs, and difficulty with his bowels and bladder. He had been previously treated with mercury from the commencement of the chancre. I saw him eighteen months after the onset of the spinal symptoms. He had spastic gait, ankle clonus, Babinski's sign, difficulty with the bladder and bowels, abdominal and cremasteric reflexes absent; no loss of sensation. It is quite possible that an infection of the spinal meninges took place when the secondary eruption occurred, that it remained latent under the influence of the mercury, and that, owing to the temporary injury caused by the fall, the virus was able to decrease the resistance of the tissues and set up active proliferation. If once the virus has obtained access to the cerebrospinal fluid, it is difficult to dislodge; under mercurial treatment, as cases show, the most remarkable results may be obtained in the relief of symptoms, and patients may be completely cured and no remissions occur. I am not, however, so hopeful about the cure of brain syphilis as I was when I finished an investigation some ten years ago on forty cases of cerebral syphilis. I have had the opportunity of seeing what became of many of those cases that I believed were either cured or permanently relieved. I regret to say not a few are dead or have had serious relapses. Brain syphilis is certainly more serious than spinal syphilis; but, as I have said before, in the majority of instances there is an affection of the whole cerebrospinal axis found post mortem in fatal cases of syphilis of the nervous system, and I speak from a large experience.

The Investigation of a Case of Suspected Syphilis or Parasyphilis of the Nervous System.

When a case presents itself we should ask ourselves and try to answer the following questions:—

(1) Do the history, signs, and symptoms point to the disease being syphilis or parasyphilis of the nervous system?

(2) Can any other cause than syphilis account for the symptoms?

(3) Does lumbar puncture show the existence of lymphocytes in the cerebrospinal fluid, and, if so, are the lymphocytes in relative abundance?

(4) Does the blood give the Wassermann reaction? Does the cerebrospinal fluid give the Wassermann reaction?

(5) What is the seat of the lesion as indicated by the signs and symptoms?

(6) Lastly and subsequently, does the result of treatment confirm our conclusions?

No doubt the clinical symptoms of syphilis of the nervous system will be fully considered by Dr. Head and others, who will take part in the discussion. I shall therefore limit my remarks especially to Questions 3 and 4.

Examination of the Cerebrospinal Fluid.

The normal fluid contains very few cellular elements, whereas in progressive parasyphilitic and syphilitic meningitic affections the lymphocytes are greatly increased in numbers. The amount of lymphocytosis is an index of the activity of the disease; it can also be used as an indication of the effect of antisyphilitic treatment. I have observed the lymphocytes diminish considerably and the signs and symptoms of the disease diminish correspondingly in cases of syphilitic meningitis.

Lymphocytosis in tabes and general paralysis does not diminish with antisyphilitic treatment, and this method is therefore useful in differentiating cases of pseudo-tabes or pseudo-general paralysis, both of which may considerably improve with antisyphilitic treatment. But lymphocytosis occurs in other affections in which syphilis and even meningitis play no part. It cannot therefore be regarded as absolutely diagnostic of a meningitis, but it is strong presumptive evidence, and, when combined with other facts, the existence of a lymphocytosis of the cerebrospinal fluid is an invaluable sign of the syphilitic and parasyphilitic affections. Particularly is it useful in deciding between a case of early doubtful general paralysis and other troubles—e.g., a patient suffering with neurasthenia and alcoholism.

In general paralysis, and to a less degree in tabes, there is also an increase in proteid in the cerebrospinal fluid. If simultaneously hæmolytic, lymphocytic, and albumin diagnostic examinations be made in the same samples of cerebrospinal fluid from the same patient, there will be found fluctuations in the degree of manifestation of their reactions, but they will always, or nearly always, be present.

The Wassermann Reaction.

In the hands of nearly all trustworthy and experienced investigators this method, introduced by Wassermann, has yielded most valuable results as a means of diagnosis. It is even claimed that for general paralysis it is more reliable than the Widal reaction for typhoid. According to Plaut, the reaction may be negative with the cerebrospinal fluid in cases of syphilis of the nervous system, but he obtained a positive result in 94 out of 95 cases of general paralysis with the cerebrospinal fluid, and in every one of the cases the serum gave a positive reaction. In cases of cerebral syphilis the serum was usually positive and the cerebrospinal fluid usually negative.

At my suggestion Dr. Henderson Smith, of the Lister Institute, and my assistant, Dr. Candler, recently examined by the Wassermann test the cerebrospinal fluid of 127 cases of various forms of insanity. Of this number, 64 were cases of general paralysis, and in 59—or 92·1 per cent.—a positive result was obtained. Of these 59 cases, 21 have since died, and the clinical diagnosis of general paralysis has been confirmed by the post-mortem investigation. Fluids from 63 cases not suffering from general paralysis were also examined, and in no single instance was a positive reaction obtained. A few of these cases have since died, but none showed at the post-mortem examination any evidence of general paralysis. Seventeen out of the 21 cases of general paralysis above referred to, which came to the post-mortem table, showed in each case before death an excess of lymphocytes in the cerebrospinal fluid. Marie and Levaditi have stated that a positive reaction by the Wassermann method does not necessarily accompany an excess of lymphocytes in the fluid, and in 5 cases in the above series of investigations, in which the Wassermann reaction was negative, there was an excess of lymphocytes in the cerebrospinal fluid. None of these patients has yet died, so that the diagnosis of general paralysis has not been absolutely confirmed. On the other hand, in 17 out of the 21 cases of general paralysis, which were verified by post-mortem investigation, the cerebrospinal fluid was examined during life, and showed an excess of lymphocytes, together with a positive Wassermann reaction.

Concerning the chemistry of the Wassermann reaction, I have found that a fluid giving a positive reaction fails to do so after the separation of the protein fraction. Noguchi has since come to the conclusion that the substance in the fluid causing the reaction is attached to the

euglobulin, from which it cannot be separated by solvents. Concerning the value of this reaction, I will give three striking examples out of many :—

(1) I recently saw a woman in one of the London County Asylums with double optic neuritis, vomiting, and headache. I had her transferred to my care at Charing Cross Hospital. Mr. Collins found five diopters of swelling in each disk. The cerebrospinal fluid did not give the Wassermann reaction, but contained abundance of lymphocytes. She was put upon mercurial inunction. The swelling of the disks rapidly subsided, and from being unable to read large print she was able to read small, the headache ceased, and the vomiting no longer occurred. She was subsequently discharged apparently cured.

(2) A man was admitted to one of the London asylums ; he improved so much that the medical officers considered it doubtful whether he was a general paralytic. Lumbar puncture was performed, and the fluid was examined by the Wassermann test ; it was positive. I expressed the opinion that it was certainly a case of general paralysis. He still continued to improve, and even his discharge was contemplated. I maintained that the test was not likely to be wrong ; the next time I visited the asylum my prediction was confirmed. He had had several seizures and within three months he was dead, and examination of the brain left no doubt about the correctness of the diagnosis.

(3) A woman, aged 34, was admitted to Charing Cross Hospital under my care, said to be suffering from tabes. There were no signs of syphilis on the body. Her youngest child is aged 4. Fifteen months ago she had a seven months' stillborn infant. Four months ago she suffered with numbness in the legs, of which she took little notice ; then she had double-vision and tingling in the feet and legs. For the past fourteen days she has suffered with a girdle sensation. She now complains of lancinating pains extending from the back down both legs, unsteadiness in gait and station, a feeling of the soles as if walking on cork, unequal pupils which reacted sluggishly to light and to accommodation, pain and cramp in the muscles of the legs, absent knee-jerks, patches of anæsthesia on the legs, and a belt of thoracic anæsthesia with girdle sensation. After inquiring into the history and finding that she had suffered with headache and squint, that the knee-jerks—which were absent on admission—had returned a few days later, I came to the conclusion that this woman, with a probable duration of infection of less than four years, was suffering really from pseudo-tabes, the result of syphilitic meningitis, especially as she told me that she had suffered

with a little stiffness of the neck, and I then obtained Kernig's sign. Lumbar puncture was performed, and 390 lymphocytes per c.mm. were found—an enormous number for tabes dorsalis. This large number of lymphocytes could only be accounted for by a widespread, active, gummatous meningitis. She was placed on mercurial inunction, and a fortnight later the lymphocytes had fallen to 70 per c.mm., and the fluid this time was tested by the Wassermann method and found to give a negative result. Unfortunately the blood was not tested on this or future occasions. A fortnight later the cerebrospinal fluid was examined and only 20 lymphocytes per c.mm. found, the patient being almost well. A fortnight later there were still no lymphocytes and the fluid was negative to the reaction. The patient was quite well; the pains, anæsthesia, and unsteadiness had entirely disappeared. She is still quite well, and twelve months have elapsed, but there is no guarantee that this woman may not have a recrudescence of symptoms; for my experience, clinical and pathological, has taught me that if once the contagion invades the subarachnoid space, producing a diffuse meningitis, symptoms of a latent affection becoming once more active may occur at any period after.

The case I have described shows the desirability of trying a mercurial cure in all cases of tabes and general paralysis in which there are atypical characters, where the Wassermann reaction is not obtained when the cerebrospinal fluid is examined and the lymphocyte reaction is marked. As clinical indications of pseudo-tabic lesions may be mentioned the following symptoms: (1) Sudden onset, or comparatively sudden onset, and rapid progress of symptoms; (2) Early appearance of affection after primary infection; (3) A variability in the condition of the tendon reflexes, especially patellar, and Achillis reflexes at one time lost, at another present, even increased and more marked on one side than the other; (4) The optic-nerve lesion causing a unilateral central scotoma, the other eye unaffected; (5) The marked improvement under treatment.

Parasyphilitic Affections: How are they Caused?

Since the discovery of the *Spirochæta pallida* and the widespread practical application of the Wassermann reaction to the diagnosis of syphilis and parasyphilis of the nervous system, new interest has been added to the problem of the pathogenesis of tabes dorsalis and general paralysis. The ætiology of these two diseases is identical: the most

characteristic physical sign—the Argyll-Robertson pupil—is common to both diseases, and is, practically speaking, met with in no other diseases. All the evidence of the ætiology of tabes and general paralysis tends to prove that there is probably one essential cause—syphilis acquired or congenital—and that there are a number of co-efficients, any one of which, by itself or in combination with others, is not capable of producing the disease. The fact that congenital syphilis leads both to tabes and general paralysis at so early a period of life as to exclude most of the contributory factors, except neuropathic heredity, is an argument in favour of syphilis being the essential cause. Moreover, since the sexes are equally affected with congenital syphilis, so males and females are affected in about equal numbers with juvenile paralysis or tabes.

Although syphilis is the essential cause, yet, as Fournier showed, these diseases are not really syphilitic, but an outcome of syphilis, and the riddle is still unsolved why only about 3·5 per cent. of the persons infected with syphilis should subsequently suffer with one of these degenerations of the nervous system, termed "Parasyphilis." But only 15 per cent. of persons suffering with diphtheria develop post-diphtheritic paralysis. These are usually cases in which the local infective process was mild and often unnoticed; in that respect, therefore, like parasyphilitic affections, which more often than not follow mild and even unrecognized primary infection and secondary symptoms. Is it because the virus is attenuated or modified, and thereby has acquired a special neurotoxic action, or is it because in a small percentage of individuals the cells of the body, *especially the cells of the nervous system*, react to the virus in a hypersensitive manner? As already indicated, there are facts which suggest the possibility of a certain form of virus with a neurotoxic action. Thus Babinski remarks that it seems possible that a syphilitic virus may sometimes be endowed with a particular aptitude for attacking the nervous system. He reports the case of two students who were infected the same day by the same woman; both died fifteen years later of general paralysis; these students were, however, related. I have recently heard of two professional men, not related, who acquired syphilis about the same time from the same nurse; ten years later they developed general paralysis. Marie and Bernard relate the instance of two men who were infected from the same source, and ten years later suffered with tabes. Erb narrates an instance of four patients infected by the same woman, who later became the subjects of either tabes or general paralyis; whilst a fifth, who had connexion with the woman but was not infected, did not suffer from any disease later. I

am indebted to my friend Dr. George Gibson for calling my attention to the following striking example given by Morel-Lavallée :—

Marthe X.

May, 1870, mistress of *Primus* (?) (Medical Student), and gave him syphilis. He died, 1873, of *syphilitic meningitis.*	December, 1871, mistress of *Secundus* (Medical Student), to whom she gave syphilis. He married later, had two healthy children, and died, 1888, of *general paralysis.*	January, 1872, lived four years with *Tertius* (Medical Student). He married later, had two healthy children, and died, 1882, of *general paralysis.*	Later, mistress of *Quartus* (Chemist). He died, 1890, of *general paralysis.*	Still later, mistress of *Quintus* (Engineer). He died (no date) of *folie syphilitique.*

Probably the most striking example supporting this theory of a special neurotoxic virus has been afforded by Brosius, who relates that seven glass-blowers suffered with chancre of the lip, and out of five who ten years later came under observation, four suffered with either tabes or general paralysis. If we accept the fact that a spirochæte is the specific causal agent of syphilis, it is conceivable that there may be varieties of this organism as there are of the malarial parasite or trypanosome. Again, the organism may become modified in its passage through the bodies of certain individuals, or it may be modified by the action of mercury. It may thus happen that the virus may vary in different cases of infection. This, however, is speculation, and not only is not supported but also is rather contraindicated so far by experiments on animals. For, although lower apes have the disease in a mild form when inoculated from the human being, yet the syphilitic virus of an infected *Macacus rhesus*, when used to infect a chimpanzee, appears to have lost none of its original virulence, for the chimpanzee suffers as badly as if it had been infected direct from the human source of the virus. We are probably therefore on more certain grounds in attributing the variations of the effects which will follow infection not to the variation of the virus but to the reaction of the individual himself; and we may represent this in the form of an equation :—

$$\text{Symptom complex } x = \frac{V}{R} = \frac{\text{virus}}{\text{resistance.}}$$

If the virus V is constant, R resistance must vary. But R is made up of a number of factors, some of which we can ascertain, but it is

generally impossible to decompose *R* into all its constituents. Roughly speaking, we may say that it is made up of what a man is born with, what has happened after birth, and what will happen in the future to resist the action of the specific virus, which in the majority of instances is of lifelong duration. Most authorities agree that with the widespread syphilization of a race for many generations, the disease tends to assume a milder form; the effects of the disease are not so severe, and a widespread tendency to an inherited immunity has been brought about. The conversion of a rural into an urban population has done much towards racial syphilization and to the diffusion of a tendency to inherited immunity and the begetting thus of a mild form of the disease. But whereas there are fewer cases of severe syphilis than formerly, there are more cases of tabes and general paralysis. The interesting description given by Col. Lambkin[1] of the syphilization of the natives of Uganda shows how severely a race previously free from this disease suffers from malignant skin, bone, and visceral disease. He also points out that parasyphilitic affections are rare, the reason being that the disease has not existed in the country for a sufficiently long time to allow of their frequent occurrence. If we consider some facts concerning congenital syphilis we must come to the conclusion that immunity is possible; how otherwise can we explain the law of Profeta—viz., that the non-syphilitic child of a syphilitic mother does not acquire syphilis from the syphilized mother who suckles it? Again, the child may be syphilitic and the mother show no sign of syphilis; nevertheless the mother does not acquire syphilis by suckling that syphilitic child, whereas a wet nurse does. In the former case the fœtus has acquired some antitoxin or something from the maternal blood which has stimulated its own tissues to react against the virus; in the latter (Colles's law) the mother has derived from the blood of the syphilized child an antitoxin or something (not the living contagium) which has stimulated her tissues to react against the virus so effectively that she cannot be infected. There is no reason to suppose that the germ cells do not participate in this reaction, seeing that every cell in the body is subjected to the sensitizing influence of the chemical products of the virus by means of the blood and lymph.

The histories I obtained in a large number of cases of juvenile general paralysis and cases of congenital syphilitic nervous disease revealed the fact that the mother very frequently had miscarriages, abortions, and typically syphilitic children without herself suffering at

[1] "System of Syphilis," ii, pp. 339-355.

all or presenting any signs of syphilis. In two instances the mother died of general paralysis; in a considerable number of instances the father died of this disease. As a general rule the history obtained from the parents of juvenile paralytics is as follows: miscarriages, abortions, dead children, children dying in infancy, often of meningitis or hydrocephalus, children who later in life suffered with nervous affections—e.g., nerve deafness, paralytic dementia, optic atrophy and tabes—and, finally, healthy children; and such a chain of circumstances would undoubtedly indicate that either the virus was becoming attenuated or the resistance to its action had been increased. In any case we may suppose that the children who were born with a syphilitic rash would be immune to reinfection, also those who afterwards suffered with parasyphilis; Krafft-Ebing's observations support this premiss. It is probably a question of degree of immunity to reinfection that would obtain in the presumably healthy children that followed the diseased ones. But this chain of events does not always occur, for sometimes children may be born with signs of heredo-syphilis after the birth of several healthy children, also parasyphilitic children may be born after the birth of several healthy children. This may be explained by the fact that the specific virus has become active again in the mother, which inference is negatived in most instances by the fact that she herself may say that she has been in good health and no signs of the disease can be discovered in her. Another explanation offers itself, and that is that the specific virus may have attacked one ovum and spared another. Levaditi has seen the spirochæte within an ovum. No two individuals, even of the same family, are born alike, because the germ plasm out of which they were formed may be similar, but is not the same; one inherits certain ancestral tendencies which the other does not; and it may happen, therefore, that a child born later than the healthy children possesses less inborn resistance to the action of the virus; and consequently manifests congenital syphilis, or later parasyphilis. How can we explain this process of decay of particular groups, systems, and communities of neurones? Why should we have optic atrophy in one individual, atrophy of the spinal portion of the sensory protoneurones in another, decay and atrophy of the cortical neurones in a third, and in many instances a decay and atrophy of the whole nervous system. We cannot suppose that it is caused by the random metastasis of the syphilitic organism in the membranes, or coats of the blood-vessels, conveyed by the lymph or blood-stream, as is probably the case in the true syphilitic lesions of the brain and spinal cord. Everything points against this, for, although parasyphilitic

affections present the most varied signs and symptoms, there is one sign usually present which is for all practical purposes only met with in parasyphilis—viz., the Argyll-Robertson pupil. No coarse random lesion will explain the constancy of this phenomenon; moreover, this condition, although a sign of syphilitic infection, does not occur in true syphilitic brain disease. Spirochætes have never been found in the cerebrospinal fluid nor antigens. Antibodies are found in abundance and probably proportional to the extent of neuronic decay in tabes and general paralysis. I think all the facts are against the views of Lesser, Bosc, Hirschl, and others, that these late manifestations of degeneration of the nervous system may be regarded as quaternary syphilis, a very late effect of the virus comparable with syphilitic orchitis, glossitis, and other sclerosing lesions. According to this view we should be compelled to consider the meningeal and perivascular infiltrations and the glia-cell proliferation as the cause of the degeneration. But there are many reasons why we cannot accept this hypothesis. The view I take of the process is that parasyphilitic disease of the nervous system depends upon two factors, intrinsic-innate, and extrinsic-acquired—the soil and the seed; the vital resistance and the specificity of the virus, $\frac{V}{R}$. All those conditions which may be inherited or acquired, and which tend to active metabolism of systems, communities, and groups of neurones functionally correlated, and which, owing to those conditions of stress which in one individual would cause spinal neurasthenia, in another cerebral neurasthenia, will, in conjunction with the stimulating effect of the syphilitic poison, cause the nerve cells to exercise an abnormal metabolic activity in the production of the side-chain molecules necessary for immunization against the toxic effects of the virus.

Ehrlich points out that we cannot suppose that the cells of the body possess *per se* an executive defensive capacity to neutralize the noxious effects of all forms of organisms, and his work on hæmolysins show that the hæmolysin for the corpuscles of a particular animal only occurs after incorporation of the molecules of those corpuscles. But we may suppose that there is an *inherent* aptitude for the cells of the body of certain individuals to readily adapt themselves to defence against the action of the syphilitic virus in a race that has been widely syphilized for generations; consequently a larger number will have a mild form of the disease.

The nerve cells are perpetual elements incapable of regeneration, highly differentiated and complex in structure and function; their centre of nutrition is the nucleus, and, when decay sets in, the retrogressive

process attacks first the fine twigs and branches and rootlets of the tree, the dendrites and dendrons; in fact, the process is an inversion of its growth and development. But what should cause this premature decay and lack of durability? For the specific energy of the whole of the neurones in the healthy body is sufficient to last until the vital spark dies out. We know the prolonged duration of infectivity of the syphilitic virus as compared with other contagious diseases, also that one attack of syphilis confers immunity during the rest of the individual's life; moreover, the experiments of Krafft-Ebing are important to remember in this respect. I may remind you that Krafft-Ebing inoculated nine general paralytics with the virus of a hard chancre, and watched them one hundred and eighty days. Not one of these developed any signs of infection, although the cases selected were those in which there was no proof of antecedent syphilitic infection. The nerve elements being perpetual, and having acquired a habit of throwing off side-chain molecules, will continue to do so during life, and will contribute largely to the immunity produced. When there is no longer metabolic equilibrium, and decay sets in, these antibodies are thrown off in increasing numbers; this seems probable from the fact that in general paralysis and tabes the quantities increase with the progress of the decay. The process of decay will manifest itself in the earliest stages by an increased irritability and functional activity of the nervous structures, often manifesting itself in a *hyperæsthesia sexualis*, and not infrequently in striking intellectual activity, followed in each case by exhaustion and loss of function.

To follow the argument further it is necessary to explain the meaning of the term "lipoid substances." They are found in all animal and vegetable cells, and are probably as important for the vital activities of protoplasm as the proteins themselves. They consist of three groups: (1) Nitrogen and phosphorus free—viz., cholesterin, fatty acids, and lipochromes; (2) cerebrosides, bodies containing nitrogen but no phosphorus, phrenosin, and kerasin; (3) phosphatides (lecithins) containing both phosphorus and nitrogen. It is probable that the cytase or complement which leads to hæmolysis in the presence of the amboceptor acts by virtue of a ferment (lipolytic) action upon the lipoid substance of cells whereby they become unloosened and liberated into the blood. It is possible that the abundant presence of these lipoids in the blood and cerebrospinal fluid may account for the exaltation and excitement so characteristic of general paralysis. Again, it is possible that the toxic effects of bacterial poisons from secondary and terminal infections may be greatly increased by the presence of these lipoid substances.

The uselessness of antisyphilitic remedies is thus easily accounted for ; indeed, they are generally positively injurious in true tabes and general paralysis, because they lower the vital energy in a system which is hypersensitive to the syphilitic virus. The only hope of doing any good is by an early diagnosis of the disease and suppression of all those exciting causes which use up the nervous energy and tend to overturn the normal metabolic equilibrium of the nervous structures. Other factors come in determining the location of the degeneration, and although microbial infections and microbial toxæmias are not directly responsible for these parasyphilitic affections, yet they may be an exciting agent to the onset of the disease, the aggravation of the symptoms, and the acceleration of the progress of neural decay.

I have often observed when influenza, dysentery, or pneumonia was prevalent in the asylums that a number of general paralytics died after a succession of epileptiform or apoplectiform seizures, and I have found post mortem that they were suffering from one of these morbid infections. Bacterial invasion, secondary or terminal infection of the organs of the body of a non-specific nature, frequently accelerate the morbid process of decay and bring about the fatal termination.

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